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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/705,457	11/02/2000	James Andya	P0998D3	7899

9157 7590 10/21/2003
GENENTECH, INC.
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SOUTH SAN FRANCISCO, CA 94080

EXAMINER

DIBRINO, MARIANNE NMN

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 10/21/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/705,457

Applicant(s)

ANDYA ET AL.

Examiner

DiBrino Marianne

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/14/03 & 3/6/03.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 37-39 and 44-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 37-39 and 44-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12, 21
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendment filed 7/14/03 (Paper No. 19) is acknowledged and has been entered.
2. Applicant's petition under 1.181, filed 3/6/03 is acknowledged and has been entered. Prosecution is hereby REOPENED.

Claims 37-39 and 44-49 are pending and are presently being examined.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 37-39, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,965,709 in view of U.S. Patent No. 4,093,606.

U.S. Patent No. 5,965,709 discloses allergy therapy (i.e., IgE-mediated disease) by administration of an anti-IgE antibody or anti-IgE fragments such as Fab or Fab' (especially col. 32, para 3), including by subcutaneous injection (especially col. 33, para 1) in amounts of about 2-3 mg/kg (especially column 33, para 4). U.S. Patent No. 5,965,709 further discloses pharmaceutical excipients which would serve as lyoprotectants such as mannitol, lactose, starch, magnesium carbonate, magnesium stearate, sodium saccharin and cellulose (especially col. 33, para 1). U.S. Patent No. 5,965,709 discloses subcutaneous or iv administration (especially column 33 at lines 12-14).

U.S. Patent No. 5,965,709 does not teach that the reconstituted formulation comprising an anti-IgE antibody is present in an amount of about 50 mg/ml to about 400 mg/ml.

U.S. Patent No. 4,093,606 discloses a reconstituted (from lyophilized form) formulation of antibody for use in treating infection in a mammal, including humans, comprising glycine, albumin and a non-ionic surfactant, the said antibody in the amount of 50 mg/ml (i.e., 5%) (especially column 3 at lines 20-23, column 1 at lines 21-32, column 5 at line 50 through column 6 at line 36).

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U.S. Patent No. 4,093,606 further discloses that the preparation can be prepared by reconstitution of lyophilized antibody in sterile water (especially column 6 at lines 26-28).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have reconstituted the anti-IgE antibody in the pharmaceutical composition disclosed by U.S. Patent No. 5,965,709 at the concentration disclosed for the antibody of the medicinal composition disclosed by U.S. Patent No. 4,093,606 for use in the method of treatment disclosed by U.S. Patent 5,965,709.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because U.S. Patent No. 5,965,709 discloses methods of treatment of human disease using a pharmaceutical composition comprising a reconstituted lyophilized antibody and lyoprotectant, and U.S. Patent No. 4,093,606 discloses a concentration of 50 mg/ml for the reconstituted antibody for use in humans.

The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

Applicant's arguments in the amendment filed 7/14/03 have been fully considered but are not persuasive.

It is Applicant's position on pages 5-8 of the said amendment that the '606 patent is concerned with a gamma globulin preparations to treat infection, and not applicable to IgE preparations and treating IgE-mediated allergic disease, and further teaches away from other than iv administration. It is Applicant's position that the '709 patent teaches IgE antagonists, and that the active ingredient is different and the treatment method is different.

It is the Examiner's position that the instant claims are drawn to a method of treatment of allergic disease using an antibody which binds IgE, not IgE antibody, and thus may be a gamma globulin, i.e., an antibody of the IgG class. It is the Examiner's further position that the '606 patent discloses use of Cohn fractions II and III which contains all of the immunoglobulins, including predominantly gamma globulins (especially column 3 at lines 59-68 and column 4 at lines 1-2). It is the Examiner's position that the '709 patent discloses use of anti-IgE antibodies in allergy therapy in vivo (especially column 32 at lines 41-44) and the preparation of such antibodies by monoclonal antibody technology which produces IgG class antibodies. With regard to the issue of iv administration, it is the Examiner's position that the '709 patent discloses subcutaneous or iv administration (especially column 33 at lines 12-14) and the '606 patent discloses iv administration of immunoglobulins. It is the Examiner's further position that the '709 patent discloses the total amount of IgG antibody which binds to IgE to be used in treatment of allergic disease either by subcutaneous or intravenous injection, and that the '606 patent discloses a concentration of IgG class antibody suitable for iv administration in humans, and that it would have been prima facie obvious to one of ordinary

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skill in the art at the time the invention was made to have administered the antibody at 50 mg/ml either subcutaneously or intravenously.

6. Claims 37-39, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,965,709 in view of U.S. Patent No. 4,093,606 and U.S. Patent No. 5,614,611.

U.S. Patent No. 5,965,709 discloses allergy therapy (i.e., IgE-mediated disease) by administration of an anti-IgE antibody or anti-IgE fragments such as Fab or Fab' (especially col. 32, para 3), including by subcutaneous injection (especially col. 33, para 1) in amounts of about 2-3 mg/kg (especially column 33, para 4). U.S. Patent No. 5,965,709 further discloses pharmaceutical excipients which would serve as lyoprotectants such as mannitol, lactose, starch, magnesium carbonate, magnesium stearate, sodium saccharin and cellulose (especially col. 33, para 1). U.S. Patent No. 5,965,709 discloses subcutaneous or iv administration (especially column 33 at lines 12-14).

U.S. Patent No. 5,965,709 does not teach that the reconstituted formulation comprising an anti-IgE antibody is present in an amount of about 50 mg/ml to about 400 mg/ml.

U.S. Patent No. 4,093,606 discloses a reconstituted (from lyophilized form) formulation of antibody for use in treating infection in a mammal, including humans, comprising glycine, albumin and a non-ionic surfactant, the said antibody in the amount of 50 mg/ml (i.e., 5%) (especially column 3 at lines 20-23, column 1 at lines 21-32, column 5 at line 50 through column 6 at line 36). U.S. Patent No. 4,093,606 further discloses that the preparation can be prepared by reconstitution of lyophilized antibody in sterile water (especially column 6 at lines 26-28).

U.S. Patent No. 5,614,611 discloses administration of anti-IgE antibodies to patients with IgE-mediated allergic disease, an amounts ranging from 1-50 mg/dose (especially column 4 at lines 44-49).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have reconstituted the anti-IgE antibody in the pharmaceutical composition disclosed by U.S. Patent No. 5,965,709 or U.S. Patent No. 5,614,611 at the concentration disclosed for the antibody of the medicinal composition disclosed by U.S. Patent No. 4,093,606 for use in the method of treatment disclosed by U.S. Patent 5,965,709.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because U.S. Patent No. 5,965,709 discloses methods of treatment of human disease using a pharmaceutical composition comprising a reconstituted lyophilized antibody and lyoprotectant, U.S. Patent No. 5,614,611 discloses use of an anti-IgE antibody for the same purpose and U.S. Patent No. 4,093,606 discloses a concentration of 50 mg/ml for the reconstituted antibody for use in humans.

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The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

Applicant's arguments in the amendment filed 7/14/03 have been fully considered but are not persuasive.

The Examiner's arguments enunciated supra apply to this rejection.

7. Claims 37-39 and 44-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al (Springer Semin. Immunopathol 1993, 15: 51-73) in view of U.S. Patent No. 5,783,186, U.S. Patent No. 4,093,606 and Cleland et al (Proceed. Intern. Symp. Control. Rel. bioact. Mater., 22 (1995), pages 514-515).

Davis et al teach administration of an anti-IgE antibody to humans to treat allergic diseases, said administration resulting in achievement of an initial plasma concentration of from 1ug/ml, to effect binding to circulating IgE and an initial plasma concentration of 10-100 ug/ml to effect binding to IgE-producing B cells. Davis et al teach that a 30-mg intravenous dose of the anti-IgE antibody CGP 51901 would be the estimated amount of antibody to achieve the former initial plasma concentration and by extension, a minimum of a 300 mg dose would achieve the latter initial plasma concentration.

Davis et al do not teach the concentration of the anti-IgE antibody, nor subcutaneous injection.

U.S. Patent No. 5,783,186 discloses administration of monoclonal antibodies to humans may be subcutaneous, intravenous or intramuscular and may be a single bolus injection. U.S. Patent No. 5,783,186 further teaches that the amount of antibody to be used will vary depending upon the nature and severity of the condition but in general will range from about 0.1 ug/kg body weight to about 100 mg/kg body weight, i.e., about 70 mg in a normal size adult, more in a heavier adult.

U.S. Patent No. 4,093,606 discloses a reconstituted (from lyophilized form) formulation of antibody for use in treating infection in a mammal, including humans, comprising glycine, albumin and a non-ionic surfactant, the said antibody in the amount of 50 mg/ml (i.e., 5%) (especially column 3 at lines 20-23, column 1 at lines 21-32, column 5 at line 50 through column 6 at line 36).

Cleland et al teach a method for providing increased stability of proteins using trehalose during lyophilization and protein concentrations of 134 mg/ml or 400 mg/ml.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the anti-IgE antibody taught by Davis et al in a single bolus as taught by U.S. Patent No. 5,783,186 at the concentration taught by U.S. Patent No.

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4,093,606 or at a higher concentration such as 100 mg/ml for administration of the monoclonal antibodies to humans, as taught by Cleland for other proteins. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a high concentration of antibody especially in the case of subcutaneous injection because the skilled artisan would have been aware that degradation of some of the injected antibody by that route of administration would limit the effective amount.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat allergic diseases as taught by Davis et al, by routes of administration taught by Davis et al or disclosed by U.S. Patent No. 5,783,186, in the total amounts taught by Davis et al or U.S. Patent No. 4,093,606 in a single bolus as taught by U.S. Patent No. 5,783,186 and because Cleland et al teach preparation of proteins at high concentrations.

The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

8. Claims 37-39 and 44-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Froehlich et al (J. Allergy Clin Immunology, Jan. 1995, IDS reference) in view of U.S. Patent No. 5,783,186 and U.S. Patent No. 4,093,606 and Cleland et al (Proceed. Intern. Symp. Control. Rel. bioact. Mater., 22 (1995), pages 514-515).

Froehlich et al teach administration of anti-IgE antibody to patients with IgE-mediated allergic disease, subcutaneously or intravenously.

Froehlich et al do not teach the concentration of antibody recited in the instant claims.

U.S. Patent No. 5,783,186 discloses administration of monoclonal antibodies to humans may be subcutaneous, intravenous or intramuscular and may be a single bolus injection. U.S. Patent No. 5,783,186 further teaches that the amount of antibody to be used will vary depending upon the nature and severity of the condition but in general will range from about 0.1 ug/kg body weight to about 100 mg/kg body weight, i.e., about 70 mg in a normal size adult, more in a heavier adult.

U.S. Patent No. 4,093,606 discloses a reconstituted (from lyophilized form) formulation of antibody for use in treating infection in a mammal, including humans, comprising glycine, albumin and a non-ionic surfactant, the said antibody in the amount of 50 mg/ml (i.e., 5%) (especially column 3 at lines 20-23, column 1 at lines 21-32, column 5 at line 50 through column 6 at line 36).

Cleland et al teach a method for providing increased stability of proteins using trehalose during lyophilization and protein concentrations of 134 mg/ml or 400 mg/ml.

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It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the anti-IgE antibody taught by Froehlich et al in a single bolus as taught by U.S. Patent No. 5,783,186 for administration of monoclonal antibodies to humans at the concentration taught by U.S. Patent No. 4,093,606 or higher or at a higher concentration such as 134 mg/ml taught by Cleland et al for administration of monoclonal antibodies to humans. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a high concentration of antibody especially in the case of subcutaneous injection because the skilled artisan would have been aware that degradation of some of the injected antibody by that route of administration would limit the effective amount.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat allergic diseases as taught by Froehlich et al, by routes of administration taught by Froehlich et al or disclosed by U.S. Patent No. 5,783,186, in the total amounts taught by Froehlich et al in a single bolus as taught by U.S. Patent No. 5,783,186 at the concentration taught by U.S. Patent No. 4,093,606 or higher concentrations achievable as taught by Cleland et al.

The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

9. Claims 37-39 and 44-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,543,144 in view of U.S. Patent No. 5,783,186 and U.S. Patent No. 4,093,606 and Cleland et al (Proceed. Intern. Symp. Control. Rel. bioact. Mater., 22 (1995), pages 514-515).

U.S. Patent No. 5,543,144 discloses treatment of patients afflicted with IgE-mediated allergy in amounts sufficient to eliminate substantially IgE-producing cells and to deplete IgE, i.e., 30-500 mg/dose/subject in humans. U.S. Patent No. 5,543,144 further discloses subcutaneous or intravenous injection of anti-IgE antibody.

U.S. Patent No. 5,543,144 does not disclose the specific concentration of the 30-500 mg dose of antibody.

U.S. Patent No. 5,783,186 discloses administration of monoclonal antibodies to humans may be subcutaneous, intravenous or intramuscular and may be a single bolus injection. U.S. Patent No. 5,783,186 further teaches that the amount of antibody to be used will vary depending upon the nature and severity of the condition but in general will range from about 0.1 ug/kg body weight to about 100 mg/kg body weight, i.e., about 70 mg in a normal size adult, more in a heavier adult.

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U.S. Patent No. 4,093,606 discloses a reconstituted (from lyophilized form) formulation of antibody for use in treating infection in a mammal, including humans, comprising glycine, albumin and a non-ionic surfactant, the said antibody in the amount of 50 mg/ml (i.e., 5%) (especially column 3 at lines 20-23, column 1 at lines 21-32, column 5 at line 50 through column 6 at line 36).

Cleland et al teach a method for providing increased stability of proteins using trehalose during lyophilization and protein concentrations of 134 mg/ml or 400 mg/ml.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the anti-IgE antibody taught by U.S. Patent No. 5,543,144 in a single bolus as taught by U.S. Patent No. 5,783,186 for administration of monoclonal antibodies to humans in the concentration taught by U.S. Patent No. 4,093,606 or higher as taught by Cleland et al for other proteins. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a high concentration of antibody especially in the case of subcutaneous injection because the skilled artisan would have been aware that degradation of some of the injected antibody by that route of administration would limit the effective amount.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat allergic diseases as disclosed by U.S. Patent No. 5,543,144, by routes of administration disclosed by U.S. Patent No. 5,543,144 or by U.S. Patent No. 5,783,186, in the total amounts disclosed by U.S. Patent No. 5,543,144 in a single bolus as taught by U.S. Patent No. 5,783,186 at the concentration disclosed U.S. Patent No. 4,093,606 or higher as taught by Cleland et al for other proteins.

The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

10. Claims 37-39 and 44-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shields et al (Int. Arch. Allergy Immunol. 1995, 107: 308-312) in view of U.S. Patent No. 5,783,186 and U.S. Patent No. 4,093,606 and Cleland et al (Proceed. Intern. Symp. Control. Rel. bioact. Mater., 22 (1995), pages 514-515).

Shields et al teaches treatment of patients afflicted with IgE-mediated allergy at doses up to 50 mg/kg in monkeys and at 0.5 mg/kg in humans of anti-IgE antibody in single or multidoses, subcutaneously or intravenously.

Shields et al does not disclose the specific concentration of the antibody.

U.S. Patent No. 5,783,186 discloses administration of monoclonal antibodies to humans may be subcutaneous, intravenous or intramuscular and may be a single bolus injection.

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U.S. Patent No. 5,783,186 further teaches that the amount of antibody to be used will vary depending upon the nature and severity of the condition but in general will range from about 0.1 ug/kg body weight to about 100 mg/kg body weight, i.e., about 70 mg in a normal size adult, more in a heavier adult.

U.S. Patent No. 4,093,606 discloses a reconstituted (from lyophilized form) formulation of antibody for use in treating infection in a mammal, including humans, comprising glycine, albumin and a non-ionic surfactant, the said antibody in the amount of 50 mg/ml (i.e., 5%) (especially column 3 at lines 20-23, column 1 at lines 21-32, column 5 at line 50 through column 6 at line 36).

Cleland et al teach a method for providing increased stability of proteins using trehalose during lyophilization and protein concentrations of 134 mg/ml or 400 mg/ml.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the anti-IgE antibody taught by Shields et al in a single bolus as disclosed by U.S. Patent No. 5,783,186 for administration of monoclonal antibodies to humans at the concentration disclosed by U.S. Patent No. 4,093,606 or higher as taught by Cleland et al for other proteins. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a high concentration of antibody especially in the case of subcutaneous injection because the skilled artisan would have been aware that degradation of some of the injected antibody by that route of administration would limit the effective amount.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat allergic diseases as disclosed by Shields et al, by routes of administration disclosed by Shields et al or by U.S. Patent No. 5,783,186, in the total amounts disclosed by Shields et al in a single bolus as taught by U.S. Patent No. 5,783,186 at the concentration disclosed by U.S. Patent No. 4,093,606 or higher as taught by Cleland et al for other proteins.

The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

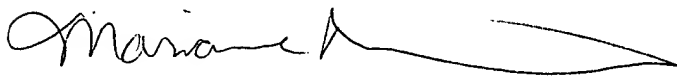
11. No claim is allowed.

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12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 703-308-0061. The Examiner can normally be reached on Monday and Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306 (before final) or 703-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
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October 17, 2003


CHRISTINA CHAN

SUPERVISORY PATENT EXAMINER
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